

Summary of investigation results

Gardenia fruit (prescription drug) and preparations containing gardenia fruit (prescription drug)

Non-proprietary name

- a. Gardenia fruit
- b. to o See Appendix.

Brand name (Marketing authorization holder)

- a. Tsumura Herbal Medicine Gardenia Fruit (Tsumura & Co.) and the others
- b. to o See Appendix.

Indications

- a. Used for formulation of Kampo medicines (Japanese traditional medicines)
- b. to o. See Appendix.

Summary of revision

- a. In the Important Precautions section, the following texts should be added:
 - (1) When using Kampo medicine (Japanese traditional medicine) containing gardenia fruit, patient's predisposition and symptoms (so-called "Sho" in Japanese in Kampo medicine), and the indication for Kampo medicine should be considered. Patients should be carefully observed and continuation of treatment should be avoided if symptoms/signs are not improved.
 - (2) When taken concomitantly with Kampo products etc., caution should be exercised regarding duplicative doses of the herbal medicines contained.

- a. to o. In the Important Precautions section, the following text should be added:
- (3) Long-term use of Kampo medicine containing gardenia fruit may result in mesenteric phlebosclerosis accompanied by abnormal colour, oedema, erosion, ulcer, and stenosis of the colon (most reported cases occurred after more than 5 years of treatment). Periodic examinations including computed tomography and large bowel endoscopy are recommended when long-term use is needed.
- a. to k. The following should be added to the Clinically Significant Adverse Reactions section:
- (4) Mesenteric phlebosclerosis

Background of the revision and investigation results

Cases of mesenteric phlebosclerosis have been reported in patients treated with gardenia fruit or Kampo medicines containing gardenia fruit in Japan. Following investigation results based on the opinions of expert advisors and the available evidence including information from literature, the MHLW/PMDA concluded that revision of the package insert was necessary.

The number of reported adverse reactions and fatal cases in the last 3 fiscal years in Japan

Mesenteric phlebosclerosis

- a. A total of 4 cases have been reported (including 4 cases in which a causal relationship with the product could not be ruled out).
- b. A total of 5 cases have been reported (including 4 cases in which a causal relationship with the product could not be ruled out).
- c. One case has been reported (causal relationship with the product could not be ruled out for this patient.).
- d. A total of 4 cases have been reported (including 2 cases in which a causal relationship with the product could not be ruled out).
- e. A total of 4 cases have been reported (including 2 cases in which a causal relationship with the product could not be ruled out).
- f. A total of 2 cases have been reported (including 1 case in which a causal relationship with the product could not be ruled out).
- g. None



This English version is intended to be a reference material for the convenience of users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

- h. None
- i. None
- j. One case has been reported*.
- k. One case has been reported*.
- l. A total of 16* cases have been reported.
- m. A total of 20* cases have been reported.
- n. A total of 4* cases have been reported.
- o. A total of 24* cases have been reported.

No fatal cases have been reported for any of a. to o.

*Causal relationship has not been evaluated.

Appendix

No.	Non-proprietary name	Brand name (Marketing Authorization Holder)	Indications
b.	Seihaito	Tsumura Seihaito Extract Granules for Ethical Use (Tsumura & Co)	Coughing accompanied by frequent expectoration
c.	Bofutsushosan	Tsumura Bofutsushosan Extract Granules for Ethical Use (Tsumura & Co) and the others	The following symptoms of those patients with thick subcutaneous fat in the abdomen and a tendency to constipation: Accessory symptoms associated with hypertension (palpitation, shoulder stiffness, and hot flushes), obesity, swelling, and constipation
d.	Shishihakuhito	Kotaro Shishihakuhito Extract Fine Granules (Kotaro pharmaceutical Co., Ltd)	Pressure sensation around the liver, jaundice, itchy sensation of the skin, or alcoholic hangover
e.	Kamikihito	Tsumura Kamikihito Extract Granules for Ethical Use (Tsumura & Co) and the others	The following symptoms of those patients with delicate constitution and poor complexion: Anemia, insomnia, mental anxiety, and neurosis

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No.	Non-proprietary name	Brand name (Marketing Authorization Holder)	Indications
f.	Ryutanshakanto	Tsumura Ryutanshakanto Extract Granules for Ethical Use (Tsumura & Co) and the others	The following symptoms of those patients with a comparatively strong constitution whose muscles in the lower abdomen are likely to become tense: Micturition pain, feeling of residual urine, turbid urine, and leucorrhea
g.	Gorinsan	Tsumura Gorinsan Extract Granules for Ethical Use (Tsumura & Co)	Frequent urination, micturition pain, and feeling of residual urine
h.	Unseiin	Tsumura Unseiin Extract Granules for Ethical Use (Tsumura & Co) and the others	The following symptoms of those patients with a sallow complexion and hot flushes: Menstrual irregularity, dysmenorrhea, automatic imbalance syndrome peculiar to women resembling climacteric disturbance, climacteric disturbance, and neurosis
i.	Keigairengyoto	Tsumura Keigairengyoto Extract Granules for Ethical Use (Tsumura & Co)	Empyema, chronic rhinitis, chronic tonsillitis, or acne
j.	Saikoseikanto	Tsumura Saikoseikanto Extract Granules for Ethical Use	The following symptoms in children who tend to be irritable: Neurosis, chronic tonsillitis, or eczema
No.	Non-proprietary name	Brand name (Marketing Authorization Holder)	Indications
k.	Seijobofuto	Tsumura Seijobofuto Extract	Acne

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No.	Non-proprietary name	Brand name (Marketing Authorization Holder)	Indications
		Granules for Ethical Use (Tsumura & Co)	
l.	Inchinkoto	Tsumura Inchinkoto Extract Granules for Ethical Use (Tsumura & Co) and the others	The following symptoms of those patients with a comparatively strong constitution and decreased urine volume who are somewhat likely to have constipation: Jaundice, hepatic cirrhosis, nephrosis, urticaria, and stomatitis
m.	Orengedokuto	Tsumura Orengedokuto Extract Granules for Ethical Use (Tsumura & Co) and the others	The following symptoms of those patients who have ruddy face with comparatively strong constitution, a touch of hot flushes, and a tendency to irritability: Nose bleeding, hypertension, insomnia, neurosis, gastritis, alcoholic hangover, climacteric disturbance and automatic imbalance syndrome peculiar to women resembling climacteric disturbance, dizziness, palpitation, eczema or dermatitis, or cutaneous pruritus

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No.	Non-proprietary name	Brand name (Marketing Authorization Holder)	Indications
n.	Shiniseihaito	Tsumura Shiniseihaito Extract Granules for Ethical Use (Tsumura & Co) and the others	Nasal congestion, chronic rhinitis, or empyema
o.	Kamishoyosan	Tsumura Kamishoyosan Extract Granules for Ethical Use (Tsumura & Co) and the others	The following symptoms of those women with delicate constitution who are easily fatigued and are apt to have stiffness shoulder, psychoneurotic symptoms including anxiety, and sometimes tendency to constipation: Oversensitivity to cold, delicate constitution, menstrual irregularity, dysmenorrhea, climacteric disturbance, and automatic imbalance syndrome peculiar to women resembling climacteric disturbance

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